

Classifying a type of brain disorder in children: an effective fMRI based deep attempt

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ABSTRACT

Recent advanced intelligent learning approaches that are based on using neural networks in medical diagnosing increased researcher expectations. In fact, the literature proved a straight-line relation of the exact needs and the achieved results. Accordingly, it encouraged promising directions of applying these approaches toward saving time and efforts. This paper proposes a novel hybrid deep learning framework that is based on the restricted boltzmann machines (RBM) and the contractive autoencoder (CA) to classify the brain disorder and healthy control cases in children less than 12 years. The RBM focuses on obtaining the discriminative set of high guided features in the classification process, while the CA provides the regularization and the robustness of features for optimal objectives. The proposed framework diagnosed children with autism recording accuracy of 91, 14% and proved enhancement compared to literature.

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1. INTRODUCTION

fMRI of brain is a representative huge information for the brain structure that details many important leadings in diagnosing diseases [1-4]. The traditional machine learning approaches lack when treating high dimensional data such fMRI and an early stage for feature preparation and extraction is necessary. Usually, an expert visualize the contents for detecting the most informative features, however, this consumes time and result a poor scalability when the data set is huge. Alternatively; the statistical methods for computerized automatic feature extraction may be used. The statistical methods prevents over-fitting but suffer from losing a portion of information and hence leads to unsatisfying accuracies [1, 4]. Accordingly, in literature, many authors tried to highlight the traditional machine learning techniques drawbacks especially in medical data [1, 3, 5]. They nominated the deep learning over the traditional techniques particularly in image classification, speech knowledge extraction and recognition, computer vision subarea, and cognitive language processing [6, 7]. Deep learning carried the automatic feature extraction phase and sophistication keeping the real meaning of data and its significant characteristics. Its architecture imitates the brain functional attitudes of the visual area [6-10]. Therefore, the application of deep learning on medical images of several diseases for feature extraction (unsupervised) and/or classification (supervised) has enhanced findings than reported by the traditional methods.

From another prospective, Autism spectrum disorder (ASD) [11], is a type of brain disorder since birth. Its symptoms affect the social behavior in addition to communication skills. More symptoms exist with variant levels such as depression, anxious, tension, and inattention to the environmental perceiving and actuating. It also causes repetitive unwanted action especially in hard situations of children's anger. The early treatments of this urgent healthcare situation provide families caring those patients with necessary support and guide their correct treatment of daily situations [11-13]. The traditional diagnosing procedure for ASD is deeply dependent on a series of interactions between children and expert specialist [12,13]. This lacks of biological evidence; require a long period of observation and analytical tests for the abnormalities in attitude and behaviors. It is a very exhausting process for children and families. Therefore, in a complement procedure to the traditional behavior based diagnoses; the fMRI has been recommended to facilitate exploring the functional characteristics of the children brains and assists as well as fasten task to get discriminative insights. The children brain is analyzed as a different complex set of regions performing different functions. These regions are globally non-segregated to process variant types of data inputs. fMRI records alter of the blood oxygen level-dependent signal to show divulge regional associations or brain networks [8-13].

In literature, many authors attempt using the ABIDE data (autism fMRI data available for researcher testing and validation of different models) for reaching optimal classification and clustering results [14-22]. This paper, proposes a new framework that deeply benefiting characteristics of the contractive autoencoder and discriminative RBM (DRBM). The contractive autoencoder highlight the most valuable features and increases data robustness and then facilities the DRBM efforts and time for classification. The work in this study was motivated to investigate whether the proposed framework will improve the results of classifying children with autism. Actually, after training the contractive autoencoder to obtain the important features and stabilize the network; the final weights efficient the learning phase of the DRBM and reduced modeling time of the tiny features in multiple areas of the image. Therefore focusing on important regions differentiating autism and healthy control is reached. The paper is organized as: section 2 presents state of the art. Section3 shows the proposed framework. Section 4, discuss results and validation. Conclusion is in Section 5.

2. STATE OF THE ART

Recently, the autism is presented and discussed in multimedia. It is frequently appears in our society and the number of children diagnosed with autism increases with notice of unsure specified clear reasons. Using artificial intelligence techniques, many researches have been trying to diagnose this disease from different data types e.g. from the video data [14] through capture the children behavior, the speech recognition [15] to save the communication of the children, and the brain imaging. In fact using machine learning approaches facilities autism diagnosis [16, 17]. In the following some related work. Chanel *et al.*, [14] detected autism through developing a mobile application. The authors used a set of 30 behavioral features (like eye movement, face smile) from 8 separate machine learning models for identifying ASD. They used 116 children home videos with autism and 46 videos of normal children and obtained accuracy of 94%. Hung-Yi *et al.*, [15] used speech signals and proposed a machine learning model for the extracted temporal information from their speech signals to categorize emotion in some patterns to determine autism. Moradi *et al.*, [23] used the support vector regression (SVR) and ENet penalized linear regression to predict symptoms of individuals with ASD. They applied their proposed model on participants of 156 ASD with ages between 8 and 40. Abbas *et al.*, [24] hybrid two classifiers based on questionnaires and behaviors extracted from videos to diagnose ASD in children of ages between year and half and six year. The authors considered language defects of those children as one of the important symptoms of ASD brain disorder. They trained their proposed language based classifier on 2299 children with ASD, 100 children with TC. They also trained their video based classifier on 3310 ASD and 585 TC children. They utilized logistic regression on both classifiers results and produced a final diagnostic screening system. Zhang *et al.*, [25] analyzed the whole brain regions connectivity using support vector machine (SVM) of children. They used the children diffusion magnetic resonance imaging (dMRI) of 70 ASD and 79 TC. They first extracted multiple diffusion features then built their classifier based on these features. Their proposed model recorded the highest accuracy of 78.33%. They also succeeded in finding the most discriminatory tracks of the brain.

Graves, *et al.*, [26], Stacked several auto-encoders (AEs) or restricted Boltzmann machine (RBMs) building a deep neural network (DNN) and applied to high-dimensional raw data. Their model architecture improved the feature learning capacity through the low-dimensional representations of the hidden layers. They proved enhanced effective model performance. Patnam *et al.*, [27] identified a deep learning based architecture using a convolutional neural network (CNN) to diagnose children with ASD self-harming behavior.

Using the multilayer of CNN, the authors extracted features while preserving spatial relationships. They reached 92% accuracy. Heinsfeld *et al.*, in [18] trained two stacked denoising autoencoders on the ABIDI data. Then, they reduced the data dimension. They used the principle components neural network for classification. Their findings include segmenting the important brain areas that are different than normal appearance and deficient function and hence used them to classify ASD from typical controls (TC) and obtained accuracy of 70%. Li, G *et al.*, in [19] proposed a multi-channel (CNN) for a classification target on (ABIDE). Abeer, *et al.*, In [1], implemented a stacked autoencoder to classify individuals with autism and recorded 70% accuracy.

Abeer, *et al.*, in [2], proposed a hybrid unsupervised and supervised framework that is based on the sparse autoencoders controlling and summarization of features and obtained better results than literature on same data domain. Xi. Li *et al.*, in [20], used two types of information exist in fMRI scans, these types reflect the spatial and temporal directions in the fMRI while training their based (CNN) model to obtain the spatial features. Then, the authors voted these features for better diagnosing results. They applied their proposed method on a sample of 82 ASD and 48 TC and enhanced results than reported in literature then. In [7], X. Guo *et al.*, introduced a deep neural network (DNN) for important feature extraction and selection. Then they used the sparse auto-encoders to summarize the whole-brain function connectivity patterns. Then, they built a DNN-FS model for classifying individuals. A sample of 55 ASD and 55 TC is used to verify their model and an accuracy of 86.36% is reported. In [8], Xi. Li *et al.*, proposed using the DNN and constructed a two phase based model. First they trained the classifier, and then they extracted the regions of interest (ROIs) of the image. They then injected these ROIs to the trained classifier to remove impurities. They selected a sample of 82 ASD and 48 TC individuals and recorded 85.3% accuracy. Khosla *et al.* [21] built a novel volumetric CNN framework that utilizes the full-resolution spatial information of fMRI images then combined with a non-linear predictive method. They used the average across majority voting and obtained precise predictions. Their model applied on 774 ABIDES-I subjects, comprising 379 ASD and 395 TCs samples. In addition, they used 393 samples from ABIDE-II (163 ASD and 230 TCs). They recorded classification accuracy above 73%. Deep neural networks (DNN) with more than one hidden layer have revealed the capability to significantly increase classification accuracy for high dimensional data by extracting lower-to-higher level information from such data through a series of neural hidden layers.

Li, *et al.*, [22] proposed a deep transfer learning neural network framework. They trained a stacked sparse autoencoder (SSAE) offline. Then, they applied the model on 4 ABIDE data-source sites of 310 subjects that contains ASD and TCs. The performance reached accuracy between 62.3% and 70.4%. Many more research findings exist; however, different perspectives still need to be investigated especially towards generalization and enhancing performance parameters. This paper was motivated by searching for a more precise classifier for autism in children taking into consideration the problems working on the fMRI image characteristics. The main objective is attempting participating valuable directions in the medical imaging knowledge discovery challenges through developing a new accurate diagnosing deep architecture. Based on that, this paper aims to benefit inheriting capabilities of a contractive autoencoder and DRBM to overcome the time factor and impulsive feature extraction of traditional methods.

3. THE PROPOSED FRAMEWORK

In this section, the necessary background needed for the proposed model is briefed. Then details of the proposed deep framework are presented

3.1. fMRI and region based segmentation

Image segmentation is a powerful approach for images in general and the medical images in specific that detects diseases or discovering difference than normal in part of the image. It is an important visualization or a pre-processing towards achieving different objectives. However, this is not an option if we process MRI medical images, where the structure details (anatomical) of for example the brain are studied. The fMRI medical image focuses on the brain functions rather than its anatomical details. In such cases, the segmentation algorithm guides efficiently towards the target using one or more of the (location, size, modification of gray matter, etc) characteristic in the multi-slices formulating each fMRI [28]. In the two-dimensional space, the fMRI consists of a number of consequent of slices (Sc_1, \dots, Sc_k). Assume a random slice of fMRI (Sc_i), Then it is referred as pixels value matrix $Sc_i(l, m)$, where $l = \{1, \dots, i\}$ and $m = \{1, \dots, j\}$. The values of the functions $S(i, j)$ are the intensity values, $I_{iv} \in \{0, \dots, 255\}$. Every I_{iv} is mapped to a one value resulted from the magnetic resonance characteristics average exists in that area of $Sc_i(l, m)$. The optimal target of segmenting slices is getting a set of similar depth, color and texture I_{iv} , or even a combination of two or more. This is intended to give different results based on the selected segmentation algorithm. The results are either labeled slice regions or a set contours. The region-based segmentation (RBS) is widely

recommended in literature [28] based on its efficiency and robustness to noise that occurred during collecting data from different sources such the case in this study where the Autism data is collected from multi-site. The region based segmentation is presented in the following assumption. Assume R_{cf} represents the whole slice as one region. Segmentation divides the connected R_{fc} into k separated sub-regions, $r_{c1}, r_{c2}, \dots, r_{ck}$, as in.(1):

$$\cup_a^k r = R_f, r_c \cap r_j = \emptyset, \forall c \text{ and } j, c \neq j \tag{1}$$

3.2. Contractive autoencoder

Particularly, the autoencoder basically [29] has an input layer, a hidden layer, and an output layer. It contains encoding and decoding process. The encoder $f(I_e)$ function is producing an abstracted version of the input I_e by a hidden layer h_e ; while the function of the decoder ($O_e(f(I_e))$) is the reconstruction process of the original input from the layer h_e with a minim loss function: $L(I_e, O_e(f(I_e)))$. The contractive autoencoder [31] used tiny derivatives and sum to an explicit regularize $\beta(h_e)$ to the hidden layer h_e and control the encoder to minimize the regularize in (2). This forced the model to discover any slight variations of input values ($\beta(h_e)$: is the squared Frobenius norm [30] of the Jacobian partial derivative matrix, α : is a free parameter)

$$\beta(h_e) = \alpha \frac{\partial f(I_e)}{\partial I_e} \tag{2}$$

3.3. Restricted boltzmann machine (RBM) and (DRBM)

RBM [31] is an bidirectional network model with a visible random variables $nr = (nr_1, nr_2, \dots, nr_i)$ and stochastic hidden variables $h = \{h_1, h_2, h_j\}$. The link between nr and h , is bidirectional. Therefore, the connection of the Unconventional h and the visible stochastic nr , center the attention on the most discriminative features [32]. This constrains compulsion neurons to belong to bipartite network and reach enhancement in the training of the model. Mathematical wise, the RBM is a probabilistic energy model aiming to obtain a probability (prob) distribution relation graph between nr and h (3), (4) and (5).

$$prob(nr) = \frac{1}{i} exp^{-E(nr)} \tag{3}$$

$$prob(nr) = \sum_{hn} prob(nr, h) = \sum_h \frac{1}{i} exp^{-E(nr, h)} \tag{4}$$

$$E(nr, h) = - \sum_{ij} \frac{1}{\sigma_i} nr_i w_{ij} h_j - \sum_i \frac{(a_i - nr_i)^2}{\sigma_i^2} - \sum_j b_j h_j \tag{5}$$

Where:

- i : a normalized term
- W_{ij} : the weights of the link ($n_i \rightarrow h_j$)
- a_i : is bias for n_i
- b_j : bias for h_j
- σ_i : is the standard deviation for the Gaussian noise for each n_i centred on a_i

In fact, the RBM appeal the weights on the responsive of a hidden unit; refare to Figure 1(a): These weights are the discriminative features of images and confirm the overall performance of the deep model. A stacked architecture of RBM is suggested targeting an enhanced version of the initial restricted Boltzmann machines. The started RBM_1 holds visible n_1 and hidden h_1 layers. Then, after training it assemblage knowledge to the followed RBM_2 by assigning its hidden layer h_1 as a visible layer $n_2=h_1$ of RBM_2 and a new hidden layer h_2 . Adding classification layer that accepts weights from h_2 , hot one labels and the back-propagating error guide a final regression layer of diagnosing the probability of being class 1 or class 2, note Figure 1 (b). The RBM is frequently used as an unsupervised model. But, adding a layer of a set of labels in some circumstances and constrains convert the model to supervised learning [32]. This is achieved when only one node o_k per class is assumed, to be =1 if the sample belongs to class k and otherwise $o_k=0$. The energy function of Gaussian visible is in (6) and (7): (e_k : a bias for o_k and s_{kj} : weight from ($h_j \rightarrow o_k$)).

$$E(nr, h, o) = \sum_j \frac{(nr_i - b_i)^2}{2\sigma_i^2} - \sum_{i,j} \frac{nr_i}{\sigma_i} w_{ij} h_j - \sum_j c_j h_j - \sum_{k,j} o_k s_{kj} h_j - \sum_k e_k o_k \tag{6}$$

$$pro(nr, h, o) = \frac{1}{n} exp^{-E(nr, h, o)} \tag{7}$$

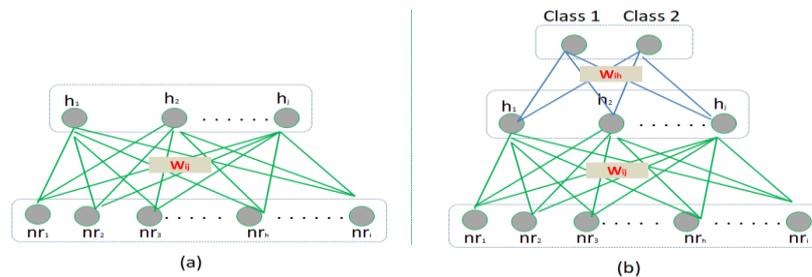


Figure 1. Different architectures of the RBM and discriminative RBM

3.4. The proposed model

This paper analyze the performance of a new developed framework of combining the contractive autoencoder and DRBM for classifying ASD and control fMRI scans in samples of children. Figure 2 shows the proposed deep framework that contains two main phases. Phase 1: obtain the fMRI ROIs after appealing region based segmentation and normalization of the fMRI slices. Then contractive autoencoder that is built of one input layer, one hidden layer, and one output layer receives such treated and preprocessed information as depicted in the Figure 2. In fact, this architecture is firstly being used for visualizing confirming the performance and quality assurance of the autoencoder. This training phase continues epochs and establishes better parameters till reaching the stable and accurate visualization level. Then the stabilized sets of weights are associated to the visible input layer of the DRBM as shown in the Figure 2. In fact, the unsupervised learning phase through the contractive autoencoder betters the generalization of the classifier.

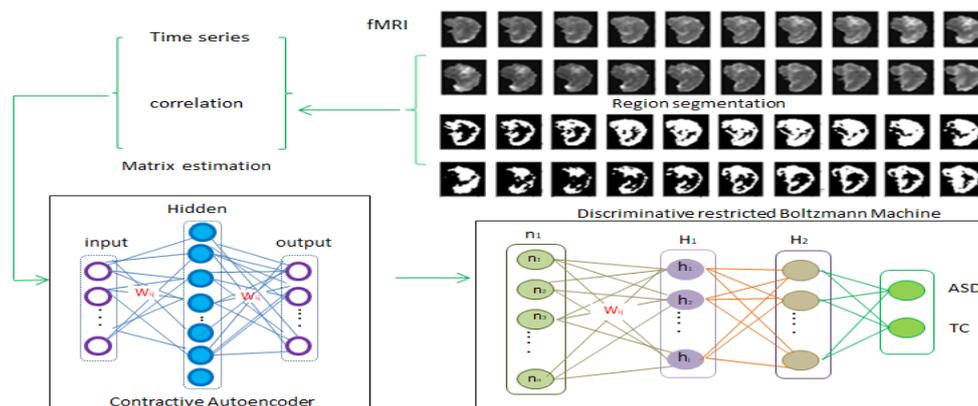


Figure 2. The proposed hybrid model

4. COMPUTATIONAL ANALYSIS AND CROSS VALIDATION

4.1. Data acquisition and preprocessing

A multi-parties neuro-imaging (abide-i) [33] and phenotypic data source for researchers available upon joining and requesting the raw data of 1,035 individuals is used in this study. It consists of near to 505 ASD and 535 TC patients. The source participants are 17 different donation sites. In fact the data is available as raw data and also a minimum preprocessed version through different pipelines offered by the autism brain imaging data exchange. In the experimental results reported in this study, the connectomes project (pcp) pipeline pre-processed version is privileged for ease of comparison of results with literature reported of the same issue. Frequent download data obtain 871 fMRI images from 1035. Some additional treatment for the data to obtain the children data subset from the whole data was performed (such normalization, soothing and age constrained selection). A choice of children age less than or equal twelve years old is extracted from whole available dataset. The number of this selected subset includes 294 individuals of ASD and TC. Different samples from different sources and its ASD and TC distribution are mentioned in Table 1. Please note that in the Table 1, the source is the site name the data is obtained, ASD-CY is children autism cases (yes autism) and TC-CN is children normal cases (no Autism). Some extra needed pre-processing for data type: e.g., the data is stored in float64 and this needs expensive computational time if compared to float32 (fMRI is usually gathered).

Accordingly and to avoid the problem of hardware resources (memory and/or processors), the sample is converted to float32. The data shape of each fMRI volume is $(61 \times 73 \times 61)$. Figure 3 shows a sample of axial, sagittal, and coronal cross representative sectional of brain fMRI (R: is right and L: is left). Figure 4, shows a multi-scan view of a random volume showing all the slices view reflection. Finally, we flattened the inputs as one dimension vector to be supplied to the deep autoencoder. Also, one-dimensional vector of labels is prepared to be given to supervised modules. We applied region-based segmentation, and then applied time series and correlation before injecting results to autoencoder. Figure 5 shows the region segmentation implemented on a sample of children fMRI and the applied contouring (region based segmentation in the upper and lower part of the figure, and contouring for TC in the upper right part of the Figure (b) ASD in the lower right part of the Figure).

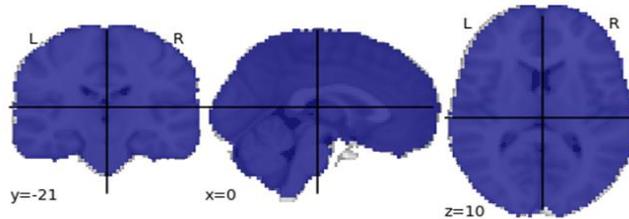


Figure 3. Axial, sagittal, and coronal cross representative sectional of fMRI (R: is right and L: is left)

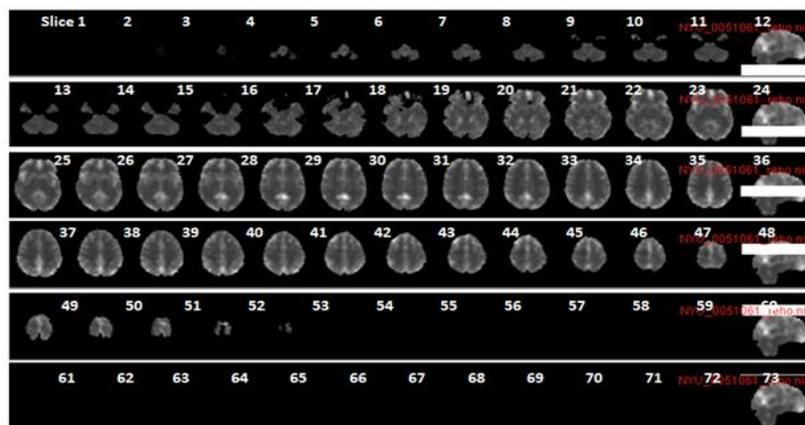


Figure 4. A random ABIDE-I fMRI showing all slices

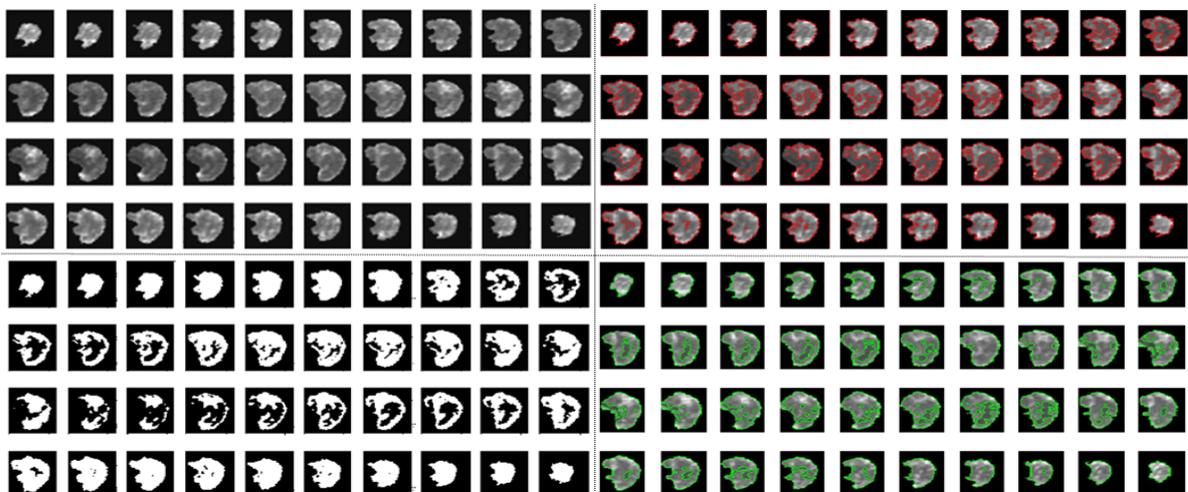


Figure 5. Sample of region based segmentation in the upper and lower part of the Figure, and sample of contouring for TC in the upper right part of the Figure (b) ASD in the lower right part of the figure

4.2. Setting parameters

We implemented the proposed model using python 3.6 and the Google colabatory (colab). A Device with Intel core i7 CPU (2.5 GHz) and 16 GB was used. The contractive Autoencoder of one input layer, one hidden and one output layer was implemented. The number of input dimensions of the proposed model is $73 \times 294 = 21462$. One normalized and smoothed slice dimension become 64×64 matrix of visible units. Note it is before normalization equals 61×61 but for smooth transfer from layer to layer, it should be easily divisible and hence is converted to matrix of 4096 nodes (64×64). This matrix is expanded to 7000 node in the hidden layer and reduced again to 4096 nodes in the output layer of the contractive autoencoder as shown in Figure 2. After stabilization of weights, it is transferred to the DRBM model. The DRBM of depths 1 was trained with learning rates of 0.01, targeting smooth and consistent performance. The stopping criteria were fixed at 60 epochs in training. Then it is set to 900 epochs for fine-tuning phase. The input dimensions is $73 \times 294 = 21462$, see Table 2. Again and as DRBM receive inpuete from the autoencndr, then the dimension of one slice is now 64×64 visible units. These are reduced to 400 nodes in the hidden layer. Additionally, the DRBM initial parameters are generated randomly from a normal distribution with mean 0 and variance $\sigma^2 = 1$. In fact, the DRBM reported start differenciante representation from epoch 13. Also, the increment in learning rate slowed down by slight change from epochs 37. The proposed method obtained an average discrminative rate or accuracy of 91.14%.

Table 2. DRBM model parameters setting

Depth	Dimension	Nodes number	Learning rate	Dropout	Function Type
Input-layer	21462	4096	-	0.5	Gaussian
Hidden-layer	-	500	0.01	0.2	-

4.3. Cross validation

For every volume of the data and for each slice, the segmentation algorithm has been applied detecting contouring of the ROIs. Then for the cross validation, these prepared data set were separated in ten folds, each of nearly thirty scans. This intends to keep balance of the class distribution of autism and normal individuals. The total sample includes 284 sample and it is almost equally distributed (148 ASD and 155 typical control). Please note sites offered less than 10 cases for children less than twelve years old as shown in table.1 (such OLIN, PITT, SDSU, TRINITY and USM) were removed during the cross validation process. Accordingly, the cross-validation accuracy for all the ten folds was obtained. In each run, one of the folds was nominated for being a test set leaving the nine folds assigned for training. Then we compute the mean accuracy values for all folds. Additionally, a leave one site cross validation was also performed. In this method, one of the folds was nominated for being a test set and the rest of folds were for training, then we repeat this procedure until all folds were involved for testing. The accuracy, sensitivity and specificity, are reported in Figure 6. Based on the fact that, the Random Forest (RF) is a traditional ensemble machine learning method that uses multiple decision trees during building its model to avoid over-fitting. This traditional method, in addition to the support vector machine (SVM) and Probabilistic NN were proposed by some authors on ABIDE-1; then comparing the proposed model in this paper with their work proves the ebenefites of the deep learaing. Table.3, shows the comparative analysis. The results nominated the proposed the deep learning framework in terms of classification accuracy in addition to generalization and scalability characteristics.

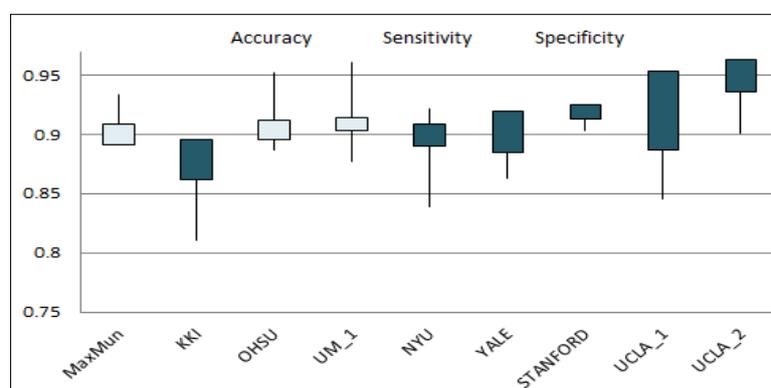


Figure 6. Accuracy, sensitivity and specificity for variant sources of the children samples

Table .3 Comparative analysis on the ABIDE-I samples with traditional and deep learning methods

Author	Iidaka, [35]	Plitt <i>et al.</i> , [36]	Chen <i>et al.</i> , [4]	Heinsfeld <i>et al.</i> , [19]	Yamagata <i>et al.</i> , [33]	Zhou <i>et al.</i> , [37]	Proposed model
Pre-processing	FC (90 ROIs-AAL atlas)	Whole brain FC(atlas)	Frequency FC	FC (CC200 ROI atlas)	Whole brain FC(atlas)	-	FC RBS
Classifier	Probabilistic NN	SVM	SVM	AE+ DNN SVM RF	LASSO Endo-phenotype	Random Tree RF	CAE+RBM
Selected data	TC ₃₂₈ , ASD ₃₁₂	TC ₅₉ , ASD ₅₉	TC ₁₂₈ , ASD ₁₁₂	TC ₅₃₀ , ASD ₅₀₅	TC ₄₅ , ASD ₁₅	TC ₁₅₃ , ASD ₁₂₇	TC ₁₅₅ , ASD ₁₄₈
Accuracy	90%	76.60%	79.20%	70% 65% 63%	78%	88%	91.14%

5. CONCLUSION & FUTURE WORK

Recent advanced intelligent learning approaches that are based on using deep learning networks in medical imaging increased researcher expectations and proved a straight-line relation of the exact needs and the achieved results. Additionally, in literature, many authors attempt using hug imaging fMRI data like the ABIDE-I (data for autism and healthy controlled samples available for researcher testing and validation of different models) for reaching optimal classification and clustering results. Accordingly, this paper was motivated by attempting a success at the challenges of the deep learning technique and the classification of the children brain autism spectrum disorder from fMRI scans. We proposed a new framework that deeply benefiting characteristic of the contractive autoencoder and discriminative RBM (DRBM). The contractive autoencoder highlighted the most valuable features and increased data robustness and then facilitated the DRBM efforts and time for classification. The work in this study investigated also whether the proposed framework improved the results of classifying children with autism in comparison with traditional techniques or different deep learning models reported on the same data. Actually, after training the contractive autoencoder to obtain the important features and stabilize the network; the final weights efficient the learning phase of the DRBM and reduced modeling time of the tiny features in multiple areas of the image. Therefore focusing on important regions differentiating autism and healthy control is reached. The computational experiments were performed on children under twelve years old from the ABIDE subset. The selected subset contains 148 ASD and 155 TC individuals from different 17 sites. The experimental results and analysis showed the challenging nature of the given problem and the effectiveness of the proposed model and reported promising improvement results rather than literature 91.14% classification accuracy. For future directions, we intend to modify the model architecture by increasing the number of hidden layers and study the effectiveness of variant parameters on the overall classification accuracy. Also we aim to investigate different segmentation algorithms for the fMRI scans as well as suggesting different deep learning frameworks.

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